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(71) Applicant (*for all designated States except US*): **REGENTS OF THE UNIVERSITY OF MINNESOTA** [US/US]; 450 McNamara Alumni Center, 200 Oak Street SE, Minneapolis, MN 55455 (US).

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(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **STEER, Clifford, J.** [US/US]; 1924 Pinehurst Avenue South, St. Paul, MN 55116 (US). **LOW, Walter, C.** [US/US]; 19845 Sweetwater Curve, Shorewood, MN 55331 (US).

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(74) Agent: **MUETING, Ann, M.**; Muetting, Raasch & Gebhardt, P.A., P.O. Box 581415, Minneapolis, MN 55458-1415 (US).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF PROMOTING CELL VIABILITY

(57) Abstract: Methods for promoting viability of a transplant cell population by administering a hydrophilic bile acid, such as ursodeoxycholic acid (UDCA), salts thereof, and analogs thereof (e.g., glyoursodeoxycholic acid and tauroursodeoxycholic acid).

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International application No.

PCT/US03/09819

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 1/00, 1/02; C12N 5/06, 5/08

US CL : 435/1.1, 1.2, 366, 375

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHEDMinimum documentation searched (classification system followed by classification symbols)
U.S. : 435/1.1, 1.2, 366, 375

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FALASCA et al. Protective Role of Tauroursodeoxycholate During Harvesting and Cold Storage of Human Liver. Transplantation. May 15 2001, Vol 71. No. 9, pages 1268-1276, especially page 1269.	1-21
X	RODRIGUES et al. Tauroursodeoxycholic Acid Partially Prevents Apoptosis Induced by 3-Nitropropionic Acid: Evidence for a Mitochondrial Pathway Independent of the Permeability Transition. Journal of Neurochemistry. 2000, Vol 75. No. 6, pages 2368-2379, especially abstract and Figure 1.	1-4
Y		5-14
X	FRIMAN et al. Ursodeoxycholic Acid Reduces Acute Rejection in Heart Allografts Rats. Transplantation Proceedings. February 1992, Vol 24. No. 1, pages 344-345.	1-3, 5
Y		4, 6-21

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

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Mall Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Vera Afremova

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/09819

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-21

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-21, drawn to a method for promoting viability of a transplant cell population by treating the cell population with hydrophilic bile acid.

Group II, claim(s) 22, drawn to a method for treating a human with Parkinson's disease by transplanting cells treated in vitro with tauroursodeoxycholic acid.

Group III, claim(s) 23-41, drawn to a method of treating a subject with Parkinson's disease by transplanting cells treated with ursodeoxycholic acid.

Group IV, claim(s) 42-53, drawn to a method of treating a donor of transplant cell population with hydrophilic bile acid.

Group V, claim(s) 54-65, drawn to a method for treating a recipient of transplant cell population with hydrophilic bile acid.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

This application contains claims drawn to more than one of permissible combinations of invention categories such as more than one of methods of using the hydrophilic bile acids.

Furthermore, the corresponding special technical features such as the use of hydrophilic bile acid compound for treating cell populations and for administration to patients are known in the prior art. For example: see abstract of the reference by Rodrigues et al. (Journal of Clinical Investigation, June 1998, 101/12, 2790-2799 Vol 101, No. 12, 2790-2799, especially abstract) that teaches the use of hydrophilic bile acid compounds for treating liver cells and for administration to prevent cell apoptosis and cell alterations. Thus, the claimed inventions lack unity.

Continuation of B. FIELDS SEARCHED Item 3:

WEST: USPT, DWPI; STN: REGISTRY, CAPLUS, MEDLINE

search terms: ursodeoxycholic acid, tauroursodeoxycholic acid, glyco-ursodeoxycholic acid, transplantation